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# Prediction of L-Asparaginase resistance in tumor therapy

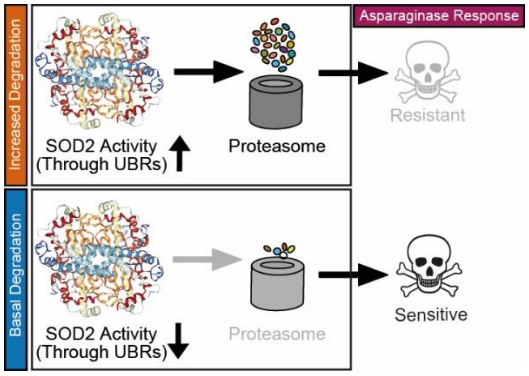
Keywords: SOD2, asparaginase, acute leukemia, drug resistance, UBR1/UBR2, cancer

## INVENTION NOVELTY

Asparaginase treatment has been a major driver of improved clinical outcomes in T-cell and B-cell acute lymphoblastic leukemias (T-ALL and B-ALL) and it also demonstrated therapeutic activity in colorectal cancers recently. However, L-Asparaginase resistance can be observed in a significant number of patients leading to a failure of treatment and resulting in a loss of time with an additional burden for patients. At present, no reliable prediction of a successful outcome of L-Asparaginase treatment is possible. The novel technology for the first time provides the possibility to predict the efficacy of L-Asparaginase treatment outcome in tumor therapy by analyzing the activity of SOD2 and/or UBR1 and/or of UBR2.

## VALUE PROPOSITION

Although L-Asparaginase treatment is a promising therapeutic approach in treatment of acute lymphoblastic leukemia and other tumor diseases the efficiency of L-Asparaginase treatment is still unpredictable. For the first time, the herewith presented diagnostic approach enables the prognosis of therapy outcome. Therefore, the novel technology perfectly complies with the urgent need for successful prediction of L-Asparaginase treatment efficacy.




*SOD2 activity and L-Asparaginase sensitivity in drug-resistant acute lymphoblastic leukemia.*

## TECHNOLOGY DESCRIPTION

Detailed studies revealed that the lack of therapeutic success in L-Asparaginase treatment is based on the activity of SOD2 and its interaction with the UBR proteins, which have been associated with the N-degron pathway. The efficacy of asparaginase induced asparagine depletion in drug resistant patients is hindered by SOD2 activity leading to activation of UBR-mediated protein breakdown and subsequent release of amino acids in tumor cells. Additional studies have shown that the inhibition of SOD2 and/or UBR proteins in ALL and colorectal tumor cells results in a significant sensitization towards asparaginase in resistant tumor cells. Thus, analysis of the activity of SOD2 and/or UBR1 and/or of UBR2 is a valuable diagnostic tool to assess the outcome of L-Asparaginase treatment. Based on this diagnostic analysis the inhibition of the key proteins UBR1 and/or UBR2 can resensitize tumor cells to L-Asparaginase therapy.

## COMMERCIAL OPPORTUNITY

In-licensing is possible.

## DEVELOPMENT STATUS

*In vitro* and *in vivo* studies have been performed at Hannover Medical School.

## PATENT SITUATION

International PCT-application (PCT/EP2023/062381) with priority of May 2022 is pending.

## FURTHER READING

Hinze L, Labrosse R, Degar J, Han T, Wagner F et al. 2020. Exploiting the Therapeutic Interaction of WNT Pathway Activation and Asparaginase for Colorectal Cancer Therapy. Cancer Discov. CD-19-1472

Hinze L, Pfirrmann M, Karim S, Degar J, McGuckin C, Vinjamur D, Sacher J, Stevenson KE, Neuberg DS, Orellana E, Stanulla M, Gregory RI, Bauer DE, Wagner FF, Stegmaier K, Gutierrez A. Synthetic Lethality of Wnt Pathway Activation and Asparaginase in Drug-Resistant Acute Leukemias. Cancer Cell. 2019 Apr 15;35(4):664-676.e7. doi: 10.1016/j.ccell.2019.03.004

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